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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/442,542	11/18/1999	LONNIE D SHEA	4100.002000	6026

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EXAMINER
KAUSHAL, SUMESH

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 07/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/442,542	SHEA ET AL.	
	Examiner	Art Unit	
	Sumesh Kaushal Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 April 2004* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-68, 102-132* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *14-18, 48, 54-65, 118-130* is/are allowed.

6)☒ Claim(s) *1-12,19-47,49-53,66-68 and 102-117* is/are rejected.

7)☒ Claim(s) *13* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's response filed on 04/26/04 has been acknowledged.

Claims 118-132 are newly filed.

Claims 1-68 and 102-132 are pending and are examined in this office action.

Applicants are required to follow Amendment Practice under revised 37 CFR §1.121. The fax phone numbers for the organization where this application or proceeding is assigned is ***703-872-9306****.*

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The references cited herein are of record in a prior Office action.

Claim Rejections - 35 USC § 103

Claims 1-12, 19-47, 49-53, 66-68, 102-117 and 131-132 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Mikos et al (US 5,514,378, 1996) and Grinstaff (5,639473, 1997) and further in view of Mineau-Hanschke (US 5,965,125 1999; filed 1995), for the same reasons of record as set forth in the office action mailed on 10/03/03.

Mikos teaches a biocompatible porous membrane structure comprising a synthetic polymer selected from group consisting of poly(alpha esters), polyanhydrides, polyorthoesters, poly(vinyl alcohol), and ethylene vinyl acetate. The cited art further teaches the use of biodegradable polymers including poly(lactic acid), poly(DL-lactic -co-glycolic acid) (PLGA). See col.3, lines 6-25; col. 23-24. The cited art further teaches making a porous polymer leaching out of a particulate from the polymer (col.6 line 41, col.7 example-1). The cited art further teaches preparation of multiplayer laminates of porous membrane using poly(L-lactic acid) and copolymers of poly(DL-

lactic-co-glycolic acid) see col.14 example-2). The cited art further teaches a porous structural matrix comprising condrocytes (col. 14, line 63-). However the cited are does not teach or suggest the incorporation of a nucleic acid segment into the structural matrix.

Grinstaff teaches biocompatible polymer composition for in-vivo gene delivery comprising a nucleic acid construct (col. 39 example-13). The cited art teaches that the biocompatible material comprises a naturally occurring polymer or a synthetic polymer or combination thereof (col.54 lines 13-18). The cited art teaches that the nucleic acid constructs are selected from IGF-1 encoding sequence, Factor VIII encoding sequence, Factor IX encoding sequence, or antisense nucleotide sequences (col. 55 lines 16-35). The cited art teaches the selection of a synthetic polymer from polyalkylene glycols, polyvinyl alcohol, polyhydroxyethyl methacrylate, polyacrylic acid, polyethyloxazoline, polyacrylamide, or polyvinyl pyrrolidinone and natural polymer selected from starch, cellulose, dextrans, alginates, chitosan, pectin, or hyaluronic acid (col.54, lines 37-67, col. 55, lines 1-18).

Mineau-Hanschke teaches a hybrid matrix composition comprising an insoluble collagen fibrils plurality of genetically engineered cells embedded in the matrix (abstract, col.1 line 55, col.19 line 25). The cited art further teaches matrix further comprises a non-collagen fibers comprising a material selected from the group consisting of nylon, dacron, polytetrafluoroethylene, polyglycolic acid, polylactic/polyglycolic acid mixture, polystyrene, polyvinylchloride copolymer, cat gut, cotton, linen, polyester and silk (col. 20 lines 56-61). The cited art further teaches the genetically engineered cells that contain an exogenous gene encoding a useful polypeptide, wherein the exogenous DNA encodes one or more medically useful polypeptides such as an *enzyme, hormone, cytokine, colony stimulating factor, angiogenesis factor, vaccine antigen, antibody, clotting factor, regulatory protein, transcription factor, receptor, or structural protein. Examples of such polypeptides include human growth hormone (hGH), Factor VIII, Factor IX, erythropoietin (EPO), albumin, hemoglobin, alpha-1 antitrypsin, calcitonin, glucocerebrosidase, low density lipoprotein (LDL) receptor, IL-2 receptor, globins, immunoglobulins, catalytic antibodies, the interleukins, insulin, insulin-like growth factor*

1 (IGF-1), parathyroid hormone (PTH), leptin, the interferons, nerve growth factors, basic fibroblast growth factor (bFGF), acidic FGF (aFGF), epidermal growth factor (EGF), endothelial cell growth factor, platelet derived growth factor (PDGF), transforming growth factors, endothelial cell stimulating angiogenesis factor (ESAF), angiogenin, tissue plasminogen activator (t-PA), granulocyte colony stimulating factor (G-CSF), and granulocyte-macrophage colony stimulating factor (GM-CSF). see Col. 2 lines 46-67, col.3 line 1-6, col.18 line 10).

Thus it would have been obvious to one ordinary skill in the art at the time of filing to modify the porous matrix of Mikos by incorporating nucleic acid sequences as taught by Grinstaff and Mineau-Hanschke. One would have been motivated to make a synthetic porous polymer comprising cells and nucleic acid molecules because in corporation of DNA molecules in the matrix structure would genetically alter the host cells at the transplantation site. One would have a reasonable expectation of success in doing so because controlling the porosity of a matrix structure and transfection of host cells around the transplantation site via DNA or DNA construct is consider routine in the art. In addition replacing a nucleic acid segment with another is an obvious variation since the cited art of record clearly teaches use of medically useful polypeptides encoded by gene of interest. Thus the invention as claimed is prima facie obvious in view of cited prior art of record.

Response to arguments

The applicant argues that Mikos does not teach or suggest the incorporation of a nucleic acid segment, a central component of the presently claimed invention. The applicant argues that Mikos in combination of two other references does not teach the invention as claimed. The applicant argues that Mikos teaches three-dimensional structures, which are simply prepared by laminating the membranes together. The applicant argues that the applicant's invention teaches away form the incorporation of nucleic in organic solvents and high temperature. The applicant argues that the structural matrices of the claimed invention are prepared from a fabrication process that involves a gas foaming/particulate leaching (GF-PL) technique that does not use organic solvents or high temperatures. The applicant argues that the polymeric shells of

Grinstaff are not, in any way, a "structural matrix" as required by the claimed invention. The applicant argues that Mineau-Hanschke is limited to hybrid matrices comprising collagen and microcapsules designed to improve the function of the collagen matrix. Mineau-Hanschke therefore has no relevance to matrices other than collagen matrices, such as matrices of synthetic polymers or alginates. The applicant argues that in the instant the specification, methods such as described in Mineau-l-lanschke are limited by the need to isolate and expand cells in vitro and by poor survival of many cell types following transplantation. The applicant argues that invention as claimed does not read upon a porous gel containing a nucleic acid segment. The applicant concluded that Mikos, Grinstaff and Mineau-Hanschke, either alone or in combination, do not teach or suggest the claimed invention.

However, applicant's argument are found NOT persuasive because subjecting nucleic acid sequences not to high temperature or organic solvents is a simple modification of the method as taught by Mikos.

In the instant case Mikos clearly teaches making a porous polymer leaching out of a particulate from the polymer (col.6 line 41, col.7 example-1). The cited art further teaches preparation of multiplayer laminates of porous membrane using poly(L-lactic acid) and copolymers of poly(DL-lactic-co-glycolic acid) see col.14 example-2). The cited art further teaches a porous structural matrix comprising condrocytes (col. 14, line 63-). In addition Mikos clearly teaches that the biocompatible porous polymer membranes are prepared by dissolving salt particles out of the membrane by immersing the membrane in water or another solvent in a water bath that is maintained at 37°C. Thus Mikos clearly suggest the use of non-organic solvent at 37°C that would lead to the preparation of biocompatible porous membrane structure, which is substantially free from residues of organic solvents (see col.3 lines 19-22; col.6, lines 41-64).

However the Mikos does not teach or suggest the incorporation of a nucleic acid segment into the structural matrix but this deficiency would have been easily corrected by considering the teaching of Grinstaff and Mineau-Hanschke, who teaches

biocompatible polymer composition for in-vivo gene delivery comprising a nucleic acid construct and genetically engineered cells.

In response to applicant's argument that combined teaching of Mikos, Grinstaff and Mineau-Hanschke, either alone or in combination, do not teach or suggest the claimed invention, the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). In instant case for the reasons as set forth above it would have been obvious to one ordinary skill in the art at the time of filing to modify the porous matrix of Mikos by incorporating nucleic acid sequences as taught by Grinstaff and Mineau-Hanschke.

In addition the scope of invention as claimed encompasses a product-by-process, wherein the invention as claimed fail to recite any structural limitation that distinguishes the claimed product over the prior art of record. Given the broadest reasonable interpretation the composition as claimed merely reads upon ***a porous gel containing a nucleic acid segment,*** which is obvious in view of the cited art of record. In the instant case the combined teaching of cited art clearly suggest the composition as claimed, since the art teaches the use of synthetic polymers in making a porous matrix comprising cells and nucleic acid segments.

The applicant fails to consider that the product-by-process claims are not limited to the manipulations of the recited steps, only the structure implied by the steps (see MPEP §2113). Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985). Even though the pores of the composition as claimed in the instant application is made by gas

foaming and leach able particulate material the final porous structure as claimed is not distinguishable from the structure as taught by the cited prior art of record. Thus the combined teaching of cited art of record clearly suggested invention as claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 131 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Newly filed claim 131 is indefinite because it recites claim limitation "substantially free from residues of organic solvent". Considering the instant specification it is unclear what are the metes and bounds of substantially free in this contest.

Conclusion

Claims 1-12, 19-47, 49-53, 66-68, 102-117 are rejected.

Claims 14-18, 48, 54-65, 118-130 are allowable.

Claims 13 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten independent form including all of the limitation of the base claim and any intervening claims.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is 571-272-0769. The examiner can normally be reached on Mon-Fri. from 9AM-5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yucel Irem Ph.D. can be reached on 571-272-0781.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to ***(571) 272-0547.***

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199. The fax phone number for the organization where this application or proceeding is assigned is **703-872-9306.**

Sumesh Kaushal
Examiner GAU 1636

JEFFREY FREDMAN
PRIMARY EXAMINER
7/02/01